

In the Claims

1 (currently amended). A method for detecting or determining the interaction of a first CFTR polypeptide with a second CFTR polypeptide, said method comprising:

(a) providing a first polynucleotide encoding a fusion protein comprising all or a portion of a first CFTR polypeptide and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable gene, wherein said first CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment said NBD1;

(b) providing a second polynucleotide encoding a fusion protein comprising all or a portion of a second CFTR polypeptide and a transcriptional activation domain of a transcriptional activator that can activate transcription of said detectable gene, wherein said second CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1;

(c) incorporating said first and second polynucleotide into a host cell comprising said detectable gene wherein transcription of said detectable gene is under control of said transcriptional activator;

(d) expressing said polynucleotide encoding said first CFTR polypeptide and expressing said polynucleotide encoding said second CFTR polypeptide under conditions in which said detectable gene is expressed when said NBD1 of said first CFTR polypeptide and said NBD1 of said second CFTR polypeptide interact; and

(e) detecting transcription of said detectable ~~marker~~ gene or expression of the gene product of said detectable gene.

2 (previously presented). The method according to claim 1, wherein said host cell is a yeast cell.

3 (previously presented). The method according to claim 2, wherein said yeast cell is *Saccharomyces*.

4 (previously presented). The method according to claim 1, wherein the host cell is a mammalian cell.

5 (previously presented). The method according to claim 1, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

6 (previously presented). The method according to claim 1, wherein one or both of said CFTR polypeptides comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

7 (previously presented). The method according to claim 1, wherein said detectable gene is selected from the group consisting of *lacZ*, *LEU2* and *HIS3*.

8 (previously presented). The method according to claim 1, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

9 (previously presented). The method according to claim 1, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

10 (previously presented). The method according to claim 1, wherein one or both of said CFTR polypeptides are mutant CFTR polypeptides.

11 (previously presented). The method according to claim 1, wherein one or both of said CFTR polypeptides comprises a mutation in said first nucleotide binding domain (NBD1).

12 (previously presented). The method according to claim 10, wherein one or both of said mutant CFTR polypeptides contains a  $\Delta F508$  mutation.

13 (previously presented). The method according to claim 1, wherein one or both of said CFTR polypeptides has a wild type CFTR amino acid sequence.

14-31 (canceled).

32 (previously presented). A method for detecting or determining the interaction of a first CFTR polypeptide with a second CFTR polypeptide, said method comprising (a) providing a fusion protein comprising all or a portion of a first CFTR protein and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable marker gene, wherein said first CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1; (b) providing a second fusion protein comprising all or a portion of a second CFTR polypeptide and a transcriptional activation domain of a transcriptional activator that can activate transcription of the detectable marker gene, wherein said second CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1; (c) contacting said first fusion protein and said second fusion protein under conditions where if said NBD1 of said first fusion protein and said NBD1 of said second fusion protein interact then said interaction causes said transcriptional activation domain to activate transcription of said detectable marker gene; and (d) detecting transcription of said detectable marker gene or expression of the gene product of said detectable marker gene.

33-35 (canceled).

36 (previously presented). The method according to claim 32, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

37 (previously presented). The method according to claim 32, wherein one or both of said CFTR polypeptides comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

38 (previously presented). The method according to claim 32, wherein said detectable gene is selected from the group consisting of *lacZ*, *LEU2* and *HIS3*.

39 (previously presented). The method according to claim 32, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

40 (previously presented). The method according to claim 32, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

41 (previously presented). The method according to claim 32, wherein one or both of said CFTR polypeptides are mutant CFTR polypeptides.

42 (previously presented). The method according to claim 32, wherein one or both of said CFTR polypeptides comprises a mutation in the first nucleotide binding domain (NBD1).

43 (previously presented). The method according to claim 41, wherein one or both of said mutant CFTR polypeptides contains a  $\Delta F508$  mutation.

44 (previously presented). The method according to claim 32, wherein one or both of said CFTR polypeptides has a wild type CFTR amino acid sequence.

45 (previously presented). A host cell comprising a polynucleotide encoding a fusion protein comprising all or a portion of a first CFTR protein and a DNA binding domain of a transcriptional activator that can bind to a site on a detectable gene, wherein said first CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1; and a polynucleotide encoding a fusion protein comprising all or a portion of a second CFTR protein and a transcriptional activation domain of a transcriptional activator that can activate transcription of said detectable gene, wherein said second CFTR polypeptide comprises a first nucleotide binding domain (NBD1) of a CFTR polypeptide, or a functional fragment of said NBD1.

46 (previously presented). The host cell according to claim 45, wherein said host cell is a yeast cell.

47 (previously presented). The host cell according to claim 46, wherein said yeast cell is *Saccharomyces*.

48 (previously presented). The host cell according to claim 45, wherein the host cell is a mammalian cell.

49 (previously presented). The host cell according to claim 45, wherein said CFTR polypeptide is a mammalian CFTR polypeptide.

50 (previously presented). The host cell according to claim 45, wherein one or both of said CFTR polypeptides comprises amino acid residue 351 through 650 of the human CFTR protein sequence.

51 (previously presented). The host cell according to claim 45, wherein said detectable gene is selected from the group consisting of *lacZ*, *LEU2* and *HIS3*.

52 (previously presented). The host cell according to claim 45, wherein said DNA binding domain comprises the DNA binding domain of GAL4 protein.

53 (previously presented). The host cell according to claim 45, wherein said transcriptional activation domain comprises the transcriptional activation domain of GAL4 protein.

54 (previously presented). The host cell according to claim 45, wherein one or both of said CFTR polypeptides are mutant CFTR polypeptides.

55 (previously presented). The host cell according to claim 45, wherein one or both of said CFTR polypeptides comprises a mutation in the first nucleotide binding domain (NBD1).

56 (previously presented). The host cell according to claim 54, wherein one or both of said mutant CFTR polypeptides contains a  $\Delta F508$  mutation.

57 (previously presented). The host cell according to claim 45, wherein one or both of said CFTR polypeptides has a wild type CFTR amino acid sequence.

58-59 (canceled).

60 (previously presented). The method according to claim 1, wherein said DNA binding domain and said transcriptional activation domain are from an organism other than yeast.

61 (previously presented). The method according to claim 12, wherein said host cell is incubated at a non-permissive temperature.

62 (previously presented). The method according to claim 1, wherein one of said CFTR polypeptides contains a  $\Delta F508$  mutation and the other of said CFTR polypeptides contains a mutation other than  $\Delta F508$ .

63 (previously presented). The method according to claim 62, wherein said host cell is incubated at a non-permissive temperature.

64 (previously presented). The method according to claim 32, wherein said DNA binding domain and said transcriptional activation domain are from an organism other than yeast.

65 (previously presented). The method according to claim 43, wherein said host cell is incubated at a non-permissive temperature.

66 (previously presented). The method according to claim 32, wherein one of said CFTR polypeptides contains a  $\Delta F508$  mutation and the other of said CFTR polypeptides contains a mutation other than  $\Delta F508$ .

67 (canceled).

68 (previously presented). The host cell according to claim 45, wherein said DNA binding domain and said transcriptional activation domain are from an organism other than yeast.

69 (previously presented). The host cell according to claim 45, wherein one of said CFTR polypeptides contains a  $\Delta F508$  mutation and the other of said CFTR polypeptides contains a mutation other than  $\Delta F508$ .